

## Draft Guidance on Empagliflozin; Metformin Hydrochloride

October 2024

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<b>Active Ingredients:</b>	Empagliflozin; Metformin hydrochloride
<b>Dosage Form:</b>	Tablet
<b>Route:</b>	Oral
<b>Strengths:</b>	5 mg; 500 mg, 5 mg; 1 gm, 12.5 mg; 500 mg, 12.5 mg; 1 gm
<b>Recommended Study:</b>	One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 12.5 mg; 1 gm  
Subjects: Healthy males and non-pregnant, non-lactating females  
Additional comments: The drug product should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 minutes for up to 4 hours after dosing. Monitor blood glucose concentrations and signs and symptoms of hypoglycemia during the study. Implement appropriate hypoglycemia management protocol.

**Analytes to measure:** Empagliflozin and metformin

**Bioequivalence based on (90% CI):** Empagliflozin and metformin

**Waiver request of in vivo testing:** The 5 mg; 500 mg, 5 mg; 1 gm, and 12.5 mg; 500 mg, strengths based on (i) the acceptable bioequivalence study on the 12.5 mg; 1 gm strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found in the FDA’s Dissolution Methods database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test product and reference listed drug (RLD).<sup>1</sup> Specifications will be determined upon review of the abbreviated new drug application.

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**Document History:** Recommended June 2016; Revised October 2024

**Unique Agency Identifier:** PSG\_206111

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<sup>1</sup> If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.